COVID-19 Treatment
Frequently Asked Questions (FAQs)
TMA COVID-19 Task Force
APRIL 27, 2020

What is the clinical presentation of patients with confirmed COVID-19?
(See Centers for Disease Control and Prevention [CDC] COVID-19: Clinical Care, 04/03/2020; CDC FAQ for Healthcare Professionals, 04/16/2020; and National Institutes of Health [NIH] COVID-19 Treatment Guidelines, 04/21/2020)

• Incubation period: median four to five days from exposure to symptoms onset (extends to 14 days).

• Signs and symptoms:
  ◦ Fever (83% to 99%)
  ◦ Cough (59% to 82%)
  ◦ Fatigue (44% to 70%)
  ◦ Anorexia (40% to 84%)
  ◦ Shortness of breath (31% to 40%)
  ◦ Sputum production (28% to 33%)
  ◦ Myalgias or muscle aches (11% to 35%)
  ◦ Loss of smell or taste
  ◦ Chills or repeated shaking with chills

• Less common symptoms (<10%):
  ◦ Headache
  ◦ Confusion
  ◦ Rhinorrhea
  ◦ Sore throat
  ◦ Hemoptysis
  ◦ Gastrointestinal symptoms: vomiting, diarrhea, nausea

• Asymptomatic and pre-symptomatic infection and transmission:
  ◦ Several studies have documented SARS-CoV-2 infection in patients who never develop symptoms (asymptomatic) and in patients not yet symptomatic (pre-symptomatic).
  ◦ Since asymptomatic persons are not routinely tested, the prevalence of asymptomatic infection and detection of pre-symptomatic infection is not well understood.
  ◦ Some data suggest that pre-symptomatic infection tended to be detected in younger individuals and was less likely to be associated with viral pneumonia.
Epidemiologic studies have documented SARS-CoV-2 transmission during the pre-symptomatic incubation period, and asymptomatic transmission has been suggested in other reports. Virologic studies also have detected SARS-CoV-2 with reverse transcription polymerase chain reaction (RT-PCR) low-cycle thresholds, indicating larger quantities of viral RNA, and cultured viable virus among persons with asymptomatic and pre-symptomatic SARS-CoV-2 infection.

The exact degree of SARS-CoV-2 viral RNA shedding that confers risk of transmission is not yet clear. Risk of transmission is thought to be greatest when patients are symptomatic, since viral RNA shedding is greatest at the time of symptom onset and declines over the course of several days to weeks.

**When is someone with COVID-19 infectious and which body fluids can spread infection?**

*(See CDC FAQ for Healthcare Professionals, 04/16/2020)*

According to the CDC, the onset and duration of viral shedding and period of infectiousness for COVID-19 are not yet known. There are reports of asymptomatic infections (detection of virus with no development of symptoms) and pre-symptomatic infections (detection of virus prior to development of symptoms) with SARS-CoV-2, but their role in transmission is not yet known. Based on existing literature, the incubation period (the time from exposure to development of symptoms) of SARS-CoV-2 and other coronaviruses (e.g. MERS-CoV, SARS-CoV) ranges from 2-14 days.

SARS-CoV-2 RNA has been detected in upper and lower respiratory tract specimens, and SARS-CoV-2 virus has been isolated from upper respiratory tract specimens and bronchoalveolar lavage fluid. SARS-CoV-2 RNA has been detected in blood and stool specimens, and SARS-CoV-2 virus has been isolated in cell culture from the stool of some patients. The duration of SARS-CoV-2 RNA detection in upper and lower respiratory tract specimens and in extrapulmonary specimens is not yet known but may be several weeks or longer. While viable, infectious SARS-CoV has been isolated from respiratory, blood, urine, and stool specimens. It is not yet known whether other non-respiratory body fluids from an infected person including vomit, urine, breast milk, or semen can contain viable, infectious SARS-CoV-2.

**Can individuals who recover from COVID-19 be reinfected with SARS-CoV-2?**

*(See CDC FAQ for Healthcare Professionals, 04/16/2020)*

The immune response, including duration of immunity, to SARS-CoV-2 infection is not yet understood. Patients with MERS-CoV are unlikely to be reinfected shortly after they recover, but it is not yet known whether similar immune protection will be observed for patients with COVID-19.

**What are the risk factors for COVID-19?**

*(See CDC COVID-19: Clinical Care, 04/03/2020; CDC FAQ for Healthcare Professionals, 04/16/2020; and CDC COVID-19 High-Risk Conditions, 04/06/2020)*

- Currently, those at greatest risk of infection are persons who have had prolonged, unprotected close contact with a patient with symptomatic, confirmed COVID-19 and those who live in or have recently been to areas with sustained transmission. For more information, see Risk Assessment (CDC, 04/19/2020).
• Age is a strong risk factor for severe illness, complications, and death. Early U.S. epidemiologic data suggests the case fatality rates to be:
  ◦ 10% to 27% in persons aged ≥85 years (highest);
  ◦ 3% to 11% for ages 65-84 years;
  ◦ 1% to 3% for ages 55-64 years; and
  ◦ <1% for ages 0-54 years.

• Based on currently available information and clinical expertise, older adults and people of any age who have serious underlying medical conditions might be at higher risk for severe illness from COVID-19.

• Based upon available information to date, those at high risk for severe illness from COVID-19 are:
  ◦ People 65 years and older
  ◦ People who live in a nursing home or long-term care facility
  ◦ People of all ages with underlying medical conditions, particularly if not well controlled, including:
    • Chronic lung disease or moderate to severe asthma
    • Heart failure
    • Cerebrovascular disease
    • Renal disease
    • Liver disease
    • Chronic kidney disease
    • Severe obesity (BMI ≥ 40)
    • Diabetes
    • Immunocompromising conditions, including cancer treatment, smoking, bone marrow or organ transplantation, immune deficiencies, poorly controlled HIV/AIDS, prolonged use of corticosteroids, and other immune-weakening medications

What is the clinical course of COVID-19?
(See CDC COVID-19: Clinical Care, 04/03/2020)

• CDC states that current research shows illness severity ranging from mild to critical:
  ◦ Mild to moderate (mild symptoms up to mild pneumonia): 81%
  ◦ Severe (dyspnea, hypoxia, or >50% lung involvement on imaging): 14%
  ◦ Critical (respiratory failure, shock, or multiorgan system dysfunction): 5%

• Among patients who developed severe disease:
  ◦ The median time to dyspnea ranged from five to eight days;
  ◦ The median time to acute respiratory distress syndrome (ARDS) ranged from eight to 12 days; and
The median time to ICU admission ranged from 10 to 12 days.

- Clinicians should be aware of the potential for some patients to rapidly deteriorate one week after illness onset.
- Among all hospitalized patients, a range of 26% to 32% of patients were admitted to the ICU, and mortality among patients admitted to the ICU ranges from 39% to 72%, depending on the study.
- The median length of hospitalization among survivors was 10 to 13 days.

**What is the recommended diagnostic testing for COVID-19?**

*(See CDC *Evaluating and Testing Persons for Coronavirus Disease 2019 (COVID-19)*, 03/24/2020 and CDC *COVID-19: Clinical Care*, 04/03/2020)*

- Infection with both SARS-CoV-2 and with other respiratory viruses has been reported, and detection of another respiratory pathogen does not rule out COVID-19.
- Diagnosis of COVID-19 requires detection of SARS-CoV-2 RNA by RT-PCR. Detection of SARS-CoV-2 viral RNA is better in nasopharynx samples compared with throat samples. Lower respiratory samples may have better yield than upper respiratory samples. Detection of SARS-CoV-2 RNA in blood may be a marker of severe illness. Viral RNA shedding may persist over longer periods among older persons and those who had severe illness requiring hospitalization (median range of viral shedding among hospitalized patients is 12-20 days). For more information on testing, please refer to TMA's COVID-19 Testing Information Frequently Asked Questions (FAQs).
- More information on specimen collection, handling, and storage is available at: CDC *Real-Time RT-PCR Panel for Detection 2019-Novel Coronavirus* (02/20/2020).

**What is the optimal imaging technique for people with COVID-19?**

*(See NIH *COVID-19 Treatment Guidelines*, 04/21/2020)*

According to NIH:

- The optimal pulmonary imaging technique for people with COVID-19 is yet to be defined.
- Initial evaluation may include chest x-ray, ultrasound, or if indicated, CT.
- Electrocardiogram should be performed if indicated.
- Laboratory testing includes a complete blood count with differential and a metabolic profile, including liver and renal function tests.
- Measurements of inflammatory markers such as C-reactive protein (CRP), D-dimer, and ferritin, while not part of standard care, may have prognostic value.

**What are the most common laboratory and radiographic findings of COVID-19?**

*(See CDC *COVID-19: Clinical Care*, 04/03/2020)*

- Lympopenia (83%)
- The following may be associated with greater illness severity:
  - Neutrophilia
Elevated serum alanine aminotransferase and aspartate aminotransferase levels
- Elevated lactate dehydrogenase
- High CRP
- High ferritin levels

- Elevated D-dimer and lymphopenia have been associated with mortality.
- Procalcitonin is typically normal on admission but may increase among those admitted to the ICU.
- Patients with critical illness had high plasma levels of inflammatory makers, suggesting potential immune dysregulation.
- Chest CT imaging commonly demonstrates bilateral, peripheral ground-glass opacities. According to the American College of Radiology (03/22/2020):
  - CT should not be used to screen for or as a first-line test to diagnose COVID-19.
  - CT should be used sparingly and reserved for hospitalized, symptomatic patients with specific clinical indications for CT.

### What is the recommended clinical management and treatment for COVID-19 in outpatient and inpatient settings?

(See CDC COVID-19. Clinical Care, 04/03/2020, and NIH COVID-19 Treatment Guidelines, 04/21/2020)

- **There is currently no specific FDA-approved treatment for COVID-19.**
- For information on the recommended clinical management and treatment for COVID-19 from NIH, see the complete NIH COVID-19 Treatment Guidelines.
- According to the CDC, the decision to monitor a patient in the inpatient or outpatient setting should be made on a case-by-case basis, taking into account the clinical presentation, requirement for supportive care, potential risk factors for severe disease, and the ability to self-isolate. For more information, see CDC Evaluating and Reporting Persons Under Investigation (PUI) (03/24/2020)
- Patients with **mild** clinical presentation (absence of viral pneumonia and hypoxia) may not initially require hospitalization, and many patients will be able to manage their illness at home.
- Patients with risk factors for severe illness should be monitored closely given the possible risk of progression to severe illness in the second week after symptom onset. Most patients with moderate to severe illness will require hospitalization.

#### Outpatient Management

(See CDC Interim Guidance for Implementing Home Care of People Not Requiring Hospitalization for COVID-19, 02/12/2020)

- Ensure appropriate infection control. For information regarding infection prevention and control recommendations, please see TMA's COVID-19 Infection Prevention and Control for Outpatient Clinics Frequently Asked Questions (FAQs).
- CDC recommends that patients evaluated in an outpatient setting who do not require hospitalization (i.e., patients who are medically stable and can receive care at home) or patients who are discharged home following a hospitalization with confirmed COVID-19 infection, may undergo home care.
• A physician should provide CDC’s *Interim Guidance for Preventing Coronavirus Disease 2019 (COVID-19) from Spreading to Others in Homes and Communities* to the patient, caregiver, and household members.

**Inpatient Management**

• Inpatient management of COVID-19 revolves around the supportive management of the most common complications of severe COVID-19:
  ◦ Pneumonia
  ◦ Hypoxemic respiratory failure/ARDS
  ◦ Sepsis and septic shock
  ◦ Cardiomyopathy and arrhythmia
  ◦ Acute kidney injury
  ◦ Complications from prolonged hospitalization, including:
    • Secondary nosocomial infections
    • Thromboembolism
    • Gastrointestinal bleeding
    • Critical illness polyneuropathy/myopathy
• Corticosteroids should be avoided unless indicated for other reasons, such as management of chronic obstructive pulmonary disease exacerbation or septic shock.

**What are the investigational therapeutics for COVID-19?**
*(See CDC *Therapeutic Options for Patients with COVID-19*, 04/13/2020, and NIH *COVID-19 Treatment Guidelines*, 04/21/2020)*

• There are no drugs or other therapeutics approved by FDA to prevent or treat COVID-19. Current clinical management involves infection prevention and control measures and supportive care, including supplemental oxygen and mechanical ventilatory support when indicated. The U.S. Department of Health and Human Services COVID-19 Treatment Guidelines Panel will soon provide interim guidelines for the medical management of COVID-19.
• Please see the *Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19 Infection* (04/11/2020) for a list of treatment recommendations and narrative summaries of other treatments undergoing evaluations.

• Current investigational agents, drugs, and therapies of note are described below.
  ◦ **Remdesivir**:
    • Remdesivir is an investigational intravenous drug with broad antiviral activity that inhibits viral replication through premature termination of RNA transcription and has in-vitro activity against SARS-CoV-2 and in-vitro and in-vivo activity against related betacoronaviruses.
    • NIH states there are insufficient clinical data to recommend either for or against using the investigational antiviral drug remdesivir for the treatment of COVID-19.
• Information about clinical trials of remdesivir is available at ClinicalTrials.gov.
• Remdesivir is also available through an expanded access program from the manufacturer, Gilead Sciences.

- **Hydroxychloroquine and chloroquine:**
  - These are oral prescription drugs that have been used for treatment of malaria and certain inflammatory conditions.
  - Both drugs are under investigation in clinical trials for pre-exposure or post-exposure prophylaxis of SARS-CoV-2 infection, and treatment of patients with mild, moderate, and severe COVID-19. More information on trials is at ClinicalTrials.gov.
  - FDA issued a Fact Sheet for Health Care Providers on the emergency use authorization to authorize use of chloroquine and hydroxychloroquine from the Strategic National Stockpile for treatment of hospitalized adults and adolescents (weight ≥50 kg) with COVID-19 for whom a clinical trial is not available or participation is not feasible.
  - FDA issued an announcement that cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems.
  - NIH states there are insufficient clinical data to recommend either for or against using chloroquine or hydroxychloroquine for the treatment of COVID-19. If chloroquine or hydroxychloroquine is used, clinicians should monitor the patient for adverse effects, especially prolonged QTc interval.
  - Except in the context of a clinical trial, NIH recommends against the use of the combination of hydroxychloroquine plus azithromycin because of the potential for toxicities.
  - Mayo Clinic has released guidance (03/25/2020) on patients at risk of drug-induced sudden cardiac death from off-label COVID-19. It includes an algorithm to assess the potential risk of drug-induced arrhythmias, which can used to modify treatment accordingly.

- **Convalescent plasma** (See FDA Recommendations for Investigational COVID-19 Convalescent Plasma, 04/08/2020; Investigational COVID-19 Convalescent Plasma - Emergency INDs Frequently Asked Questions, 04/03/2020; and NIH COVID-19 Treatment Guidelines, 04/21/2020):
  - NIH states there are insufficient clinical data to recommend either for or against the use of convalescent plasma or hyperimmune immunoglobulin for the treatment of COVID-19.
  - Because there are no approved treatments, FDA is permitting the emergency investigational use of convalescent plasma to treat COVID-19 under the criteria of the emergency investigational new drug (eIND).
  - FDA has issued guidance for health care providers and investigators on the administration and study of investigational convalescent plasma collected from individuals who have recovered from COVID-19 (COVID-19 convalescent plasma) during the public health emergency. The guidance provides recommendations on the following:
    - Pathways for use of investigational COVID-19 convalescent plasma
    - Patient eligibility
° Collection of COVID-19 convalescent plasma, including donor eligibility and donor qualifications
° Labeling
° Recordkeeping

• Physicians should contact their local blood center to inquire about obtaining convalescent plasma from a recovered donor through a single-patient eIND. Information on how to request an eIND is on the FDA website.
• FDA does not collect COVID-19 convalescent plasma or provide COVID-19 convalescent plasma.

° Other drugs: Several other drugs (e.g., investigational antivirals; immunotherapeutic, host-directed therapies) are under investigation in clinical trials or are being considered for clinical trials of pre-exposure prophylaxis, post-exposure prophylaxis, or treatment of COVID-19 in the U.S. and worldwide. Information on registered clinical trials for COVID-19 in the U.S is available at ClinicalTrials.gov.

• The Milken Institute is currently tracking (04/20/2020) the development of treatments and vaccines for COVID-19, providing a document that contains an aggregation of publicly available information from validated sources.
• In the absence of an approved vaccine, community mitigation measures and adherence to recommended infection prevention and control measures are the ways to reduce SARS-CoV-2 transmission among persons in the community and in health care facilities.

What are the recommendations for pre- or post-exposure prophylaxis treatment?
(NIH COVID-19 Treatment Guidelines, 04/21/2020)

• According to NIH, at present, no agent is known to be effective for preventing SARS-CoV-2 infection before an exposure (i.e., as PrEP) or after an exposure (i.e., as PEP).
• The NIH does not recommend the use of any agents for pre-exposure prophylaxis (PrEP) against SARS-CoV-2 outside of the setting of a clinical trial.

When can you advise the patient to discontinue transmission-based precautions or home isolation?
(See CDC Interim Guidance for Discontinuation of Transmission-Based Precautions and Disposition of Hospitalized Patients with COVID-19, 03/23/2020, and CDC Interim Guidance for Discontinuation of In-Home Isolation for Patients with COVID-19, 02/12/2020)

1. Test-based strategy.
° Resolution of fever without the use of fever-reducing medications, and
° Improvement in respiratory symptoms (e.g., cough, shortness of breath), and
° Negative results of an FDA Emergency Use Authorized COVID-19 molecular assay for detection of SARS-CoV-2 RNA from at least two consecutive nasopharyngeal swab specimens collected ≥24 hours apart (total of two negative specimens).
2. Non-test-based strategy.

- At least three days (72 hours) have passed since recovery – defined as resolution of fever without the use of fever-reducing medications and improvement in respiratory symptoms (e.g., cough, shortness of breath); and,
- At least seven days have passed since symptoms first appeared.

A test-based strategy is preferred for discontinuation of transmission-based precautions for patients who are

- Hospitalized;
- Severely immuno-compromised; or
- Being transferred to a long-term care or assisted living facility.

If testing is not readily available, facilities should use the non-test-based strategy for discontinuation of transmission-based precautions or extend the period of isolation beyond the non-test-based-strategy duration, on a case-by-case basis in consultation with local and state public health authorities.

For health care personnel, see CDC Return to Work Criteria for HCP with Confirmed or Suspected COVID-19, 04/13/2020.

How is COVID-19 treatment reimbursed?

- Visit TMA's Practice Help page for information on COVID-19 testing and treatment reimbursement, including:
  - Telemedicine;
  - Payers/Insurance; and
  - Billing and Coding

AMA: Special coding advice during COVID-19 public health emergency.

For other information not addressed in this FAQ, please refer to the following resources:

CDC Coronavirus COVID-19 website

TMA COVID-19 Resource Center

DSHS Coronavirus Disease (COVID-19) website

CDC 24/7 COVID-19 Clinician Guidance Hotline at (770) 488-7100

DSHS COVID-19 Call Center at (877) 570-9779, Monday-Friday, 8 am-6 pm; Saturday-Sunday, 8 am-5 pm

DSHS 24/7 Hotline at (888) 963-7111 and email: coronavirus@dshs.texas.gov

TMA Knowledge Center (800) 880-7955 or knowledge@texmed.org